REMARKS

I. The Office Action

Claims 1-16 and 26-40 were withdrawn from consideration. The Office objected to claims 24 and 25 for assertedly failing to further limit the subject matter of a previous claim. Claims 17-25 were rejected under 35 U.S.C. § 112, second paragraph, for assertedly being indefinite. Claims 17-25 also were rejected under 35 U.S.C. § 101 for assertedly being directed to non-statutory subject matter. Claims 17-19, 24, and 25 were rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Sawada et al., *J. Exp. Med.*, *187*(9), 1439-1449 (1998) ("Sawada"). Claims 17-25 were rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Petit et al., *Nature Immunology*, *3*(7), 687-694 (2002) ("Petit"), and under 35 U.S.C. § 103(a) as assertedly being obvious in view of Sawada taken with Lapidot et al., *Leukemia*, *16*(1), 1992-2003 (2002) ("Lapidot"). Reconsideration of these rejections is respectfully requested.

II. Pending Claims and Claim Amendments

Claims 17-25 have been amended to recite an "isolated population of stem cells." Claim 17 has been amended to recite that the stem cells comprise a transgene encoding CXCR, and to clarify that the population comprises a high amount of immature primitive progenitor cells. Claims 18-25 also have been amended to simplify the claim language. The claim amendments are supported by the specification at, e.g., page 11, lines 5-14; page 12, line 31, through page 13, line 3; page 15, lines 3-7; and page 27, lines 14-17. No new matter has been added by way of the amendments. Claims 1-40 are pending, and claims 17-25 are currently under examination.

III. Claims 24 and 25 Are Proper Dependent Claims.

The Office objected to claims 24 and 25 for assertedly failing to further limit the subject matter of claim 17 by reciting limitations that do not affect the structure of the claimed cell population. Claims 24 and 25, however, further define the stem cells of the isolated population by defining the low and high concentrations of SDF-1 to which the stem cells demonstrate improved CXCR4 signaling capacity. Claims 24 and 25 are, thus, proper

dependent claims under 35 U.S.C. § 112, fourth paragraph, and the objection should be withdrawn.

IV. The Rejection Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn.

Claims 17-25 were rejected under 35 U.S.C. § 112, second paragraph, for assertedly failing to particularly point out and distinctly claim the invention. The rejection is respectfully traversed.

The Office addressed only claims 17-19 and 23-25 in the Section 112, second paragraph, rejection. The bases for rejection pertain to specific claim language that is not present in claims 20-22, and thus the rejection does not apply to those claims. Because no basis has been alleged for rejecting claims 20-22, the rejection of these claims was improper, and should be withdrawn. The Office rejected claim 17 as assertedly being indefinite for reciting "stem cells expressing a high amount of immature primitive progenitors." Claims 18 and 19 were rejected for assertedly lacking antecedent basis. The rejection is moot in view of the amendments to claims 17-19.

In addition, the Office rejected claims 23-25 for assertedly reciting unclear numerical ranges. As amended, claim 23 defines the high amount of $CD34^{+}/CD38^{-/low}$ cells in the population as at least about 3% of the population. Amended claim 24 defines the low concentration of SDF-1 as less than or equal to 50 ng/ml, and amended claim 25 defines the high concentration of SDF-1 as at least about 1 microgram/ml. The Office contends that claims reciting "at least about" are indefinite where there is close prior art and there is nothing in the specification, prosecution history, or prior art to provide any indication as to what range of activity is covered by the term "about."

First, it is well established that claims may contain relative terminology, and the Board of Patent Appeals and Interferences has held that the phrase "at least about" does not automatically render a claim indefinite. *Ex Parte Peck*, 2009 WL 211768, *8 (Bd. Pat. App. & Interf.). In *Peck*, the Board reversed a Section 112, second paragraph, rejection of a claim reciting "at least about five-fold," and agreed that "the phrase *about five-fold* provides for tolerances above and below five-fold, and the phrase *at least* means that those tolerances

provide the minimum values . . . [t]here is nothing indefinite in the juxtaposition of those two phrases to form the phrase 'at least about'" (emphasis in original).

The Office cited *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991), as support for the rejection of claims 23-25. The Federal Circuit in *Amgen* found the phrase "at least about" indefinite in view of close prior art and the inherent imprecision in measuring the claim feature modified by the term "about." *Id.* at 1217-18. The instant situation is distinguishable from *Amgen* in at least two respects. First, the Office failed to identify "close prior art" in the Section 112, second paragraph, rejection. The art cited with respect to the Section 102 and 103 rejections is not "close prior art" with respect to the specifically recited features of claims 23-25 which are at issue here. The claim at issue in *Amgen* was directed to homogenous erythropoietin (EPO) having a specific activity of "at least about 160,000 IU." *Id.* at 1217. Original claims in the underlying patent application recited an EPO specific activity of "at least 120,000," but were cancelled during prosecution in view of "close prior art" disclosing EPO having a specific activity of 128,620 IU. The patent examiner noted that recitation of the specific activity of "at least 160,000 IU" patentably distinguished subsequently allowed claims from the "close prior art." *Id.* at 1217-1218; *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 1989 WL 169006. *65 (D. Mass).

Here, the cited references do not teach or suggest the subject matter of amended claims 23-25 so as to cast uncertainty as to the scope of the claims to which Applicants are entitled. Indeed, the cited art does not teach or suggest an isolated population of stem cells comprising a transgene encoding CXCR, wherein the stem cells exhibit improved CXCR4 signaling capacity in response to an SDF-1 concentration less than or equal to 50 ng/ml or at least about 1 μg/ml, as recited in the alternative claims 24 and 25, respectively. The cited art also does not teach or suggest such an isolated population of cells wherein $CD34^{+}/CD38^{-/low}$ cells represent at least about 3% of the population, as recited in claim 23. The cited references do not constitute "close prior art" that would prohibit the use of the relative claim language in claims 23-25.

Second, assays for determining the percentage of $CD34^{+}/CD38^{-/low}$ cells in a population and SDF-1 concentrations are not as imprecise as the bioassays required to measure specific activity in *Amgen*. The lower court found that the claim feature "at least

160,000 IU" reflected a range of error of between 20% and 30% as recognized by the scientific community to be inherent in the bioassay. *Amgen,* 1989 WL 169006 at *74. The range of error inherent to the specific activity feature, coupled with the relative term "about," rendered the claim indefinite. *Amgen*, 927 F.2d at 1217. In contrast, the percentage of a subpopulation of cells can be more precisely determined using, e.g., fluorescence-activated cell sorting. Likewise, SDF-1 concentrations can be determined using highly reliable laboratory techniques, such as an enzyme-linked immunosorbent assay (ELISA). As the claimed feature can be more precisely measured, use of relative terminology does not render the claim indefinite. See, e.g., *Ex Parte Heck*, 2008 WL 4266205 (Bd. Pat. App. & Interf.) (reversing a rejection of a claim reciting a polynucleotide sequence having "at least about 98% identity" to a reference sequence for alleged indefiniteness because, in part, sequence identity can be precisely determined).

For the reasons set forth above, the rejection of claims 17-25 under Section 112, second paragraph, have been overcome or rendered moot, and should be withdrawn.

V. The Rejection Under 35 U.S.C. § 101 Should Be Withdrawn.

The Office rejected claims 17-25 under Section 101 for assertedly being drawn to non-statutory subject matter. According to the Office, the claims encompass a human being and immature stem cells produced normally during differentiation. Claims 17-25 have been amended to recite an isolated population of stem cells comprising a transgene encoding CXCR4. Thus, the claims do not encompass a human being or a naturally occurring population of stem cells. Accordingly, Applicants respectfully request withdrawal of the Section 101 rejection.

VI. The Rejections Under 35 U.S.C. § 102(b) Should Be Withdrawn.

The Office rejected claims 17-25 under Section 102(b) as assertedly being anticipated by Sawada and/or Petit. The rejection is respectfully traversed for the reasons set forth below.

A reference anticipates the pending claims *only* if the reference teaches *each and every element* of the pending claims. See, e.g., *Verdegaal Bros. v. Union Oil Co. of*

California, 814 F.2d 628, 631 (Fed. Cir. 1987). Neither Sawada nor Petit teach every feature of the claimed isolated cell population.

The Office contends that claims 17-19, 24, and 25 are anticipated by Sawada, which purportedly describes a transgenic mouse comprising a human CXCR4 gene. Claim 17 has been amended to recite an isolated population of stem cells comprising a transgene encoding CXCR4. A transgenic mouse is *not* an isolated population of cells. The *in vitro* experiment described in Sawada utilized purified thymocytes, not stem cells, to identify mechanisms of HIV infection of lymphocytes (i.e., mature immune cells) (see, e.g., page 1440, paragraph bridging columns 1 and 2; and page 1441, column 2, first full paragraph). The reference does not teach or suggest an isolated stem cell population, much less an isolated population of stem cells comprising a CXCR4 transgene. Because the reference does not disclose each element of any pending claim, the Section 102(b) rejection cannot stand.

Claims 17-25 were rejected for assertedly being anticipated by Petit, which purportedly describes naturally occurring immature stem cells. According to the Office, claim 17 characterizes the stem cells as being *prepared by* introducing into the stem cells a DNA fragment comprising the sequence of CXCR4, but does not require the stem cells to *maintain* the CXCR4 sequence. Thus, the Office asserts that the stem cells of the claimed isolated population are indistinguishable from immature stem cells produced during the normal differentiation process. (Office Action, page 9.) Claim 17 has been amended to recite that the stem cells of the isolated population comprise a transgene encoding CXCR4. Petit does not teach (or even suggest) transducing stem cells with a transgene encoding CXCR4. Thus, the reference does not anticipate the pending claims under Section 102(b).

For the reasons set forth above, neither Sawada nor Petit discloses each and every element of the pending claims, and the anticipation rejection should be withdrawn.

VII. The Rejection Under 35 U.S.C. § 103(a) Should Be Withdrawn.

The Office rejected claims 17-25 under Section 103(a) as assertedly being unpatentable over Sawada taken with Lapidot. The rejection is respectfully traversed; the cited references do not render obvious the subject matter of the amended claims.

Sawada purportedly describes a transgenic mouse comprising a human CXCR4 gene, which the Office interprets as disclosing a cell population comprising stem cells having the CXCR4 gene. (Office Action, page 11.) However, the pending claims are directed to an *isolated* population of stem cells comprising a transgene encoding CXCR4. One of ordinary skill in the art would not understand a transgenic mouse to be an "isolated" population of cells, and disclosure of a transgenic animal comprising a large genus of cell types does not suggest an isolated stem cell population. See, e.g., M.P.E.P. 2144.08, Part II ("The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F.3d 380, 382, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994) ('The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.')"). In *Baird*, the Office rejected a claim directed to three chemical compounds under Section 103 in view of a prior art reference disclosing a generic formula encompassing a vast number of chemical compounds (including the three claimed compounds) and a few species falling within the scope of the generic formula. *Id.* at 381-383. The Federal Circuit found the claim to the undisclosed species to be patentable over the prior art reference, stating "[a] disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds." *Id.* at 383. Here, Sawada does not teach a particular reason to select a cell population comprising *stem cells* comprising a CXCR4 transgene. To the contrary, the purpose of the study described in Sawada is to determine if chemokine receptors render mouse *primary lymphocytes* susceptible to HIV infection (see, e.g., the paragraphs bridging pages 1439-1440, and pages 1443-1444). The only disclosure in Sawada relating to an isolated cell population is limited to mouse thymocytes (not, e.g., hematopoietic stem cells) exposed to HIV and assayed for antigen production (see, e.g., page 1441, column 2, first full paragraph). One of ordinary skill would not have been motivated to generate an isolated cell population comprising a high amount of immature primitive progenitor stem cells, as presently claimed, to study HIV infection in T-cells.

Lapidot does not cure the deficiencies of Sawada as a reference cited against the pending claims. The Office cites Lapidot as supplementing the disclosure of Sawada with respect to the subject matter of claims 21-23. In particular, the Office acknowledges that

Sawada does not disclose a cell population comprising $CD34^+/CD38^{-/low}$ progenitor cells, but asserts that one of ordinary skill would deduce that the cell population of Sawada contains $CD34^+/CD38^{-/low}$ progenitor cells in view of Lapidot's purported teaching that "cord blood contains primitive $CD34^+/CD38^{-/low}$ stem cells which are up to 5% of total $CD34^+$ cells." Lapidot does not teach or suggest a cell population comprising CXCR4-transduced stem cells. Furthermore, the reference's general discussion of stem cell subpopulations cited by the Office would not motivate one of ordinary skill to modify the teachings of Sawada. As noted above, Sawada seeks to determine HIV infectivity of primary lymphocytes, not stem cells or subpopulations of stem cells. There is nothing in the references, alone or in combination, that suggests an isolated population of stem cells comprising a transgene encoding CXCR4 and exhibiting improved CXCR4 signaling capability in response to low and/or high concentrations of SDF-1, wherein the isolated population comprises a high amount of immature primitive progenitor cells.

Sawada and Lapidot, alone and in combination, fail to render obvious the claimed isolated population of stem cells. Accordingly, the Section 103 rejection should be withdrawn.

VIII. Conclusion

In view of the above amendments and remarks, Applicants believe that the pending application is in condition for allowance. The Office is invited to contact the undersigned attorney by telephone if there are issues or questions that might be efficiently resolved in that manner.

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Respectfully submitted,

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